

tering sound of the murmur of mitral contraction. It is usually short and rather blowing in character. But it may partake somewhat of the well-known quality, and in Case III. this circumstance, conjoined with the smallness of the pulse, led me to diagnose a stenosis which the post-mortem examination proved to be absent. In Case I. the presystolic murmur was long and quite typical, and was even reported to have been accompanied by a thrill (this, however, was not present while the case was under my own observation). It is unfortunate that in this case the condition of the heart nine months afterward threw some doubt on the accuracy of the record of the post-mortem examination. But if any stenosis existed, it must have been very slight, and the aortic regurgitation gave rise to the most extreme and characteristic symptoms. In the light of the other cases I have no doubt that the presystolic murmur was in great part, if not entirely, due to the aortic regurgitation. It is worthy of note that in this case there was a large vegetation below the anterior cusp of the aortic valve and vegetations also on and below the right posterior cusp; hence the regurgitant stream was probably mainly directed toward the left, and it would therefore strike the anterior mitral flap. Similarly, in Case IV., the anterior and right posterior cusps of the aortic valve were actually united along their margin, leaving the left half of the orifice alone patent, and in Case II. the pathological process had gone on to completely calcified union of the cusps, leaving again as patent opening only the left portion of the normal orifice. Hence, in all these three cases the regurgitant stream must have impinged on the anterior mitral flap, and there is no difficulty in seeing how this flap was in consequence thrown into vibrations when it was carried outward by the incoming current through the mitral orifice at the end of the diastole. For, "in full diastole" (to quote Dr. McAlister's account of the observations of Ludwig and Hesse, *British Medical Journal*, 1882, vol. ii. p. 825), "the flap and its cords are stretched aslant across the cavity. . . . The flap does not hang loosely down; it is stretched taut from basal ring to muscle-tip." Hence under the influence of two independent blood-currents impinging on its opposite sides vibrations are easily produced and give rise to a murmur during the ventricular diastole, more especially during its closing period, which corresponds with the systole of the auricle.

THE THEORY OF PYREXIA.

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DURING the last ten years much importance has been attached to the part played by the nervous system in the production of pyrexia. Many

observers have put upon record cases in point. Six years ago I published several such,¹ and have since, from time to time, mentioned others.² In America³ Ott has given the profession some valuable material bearing on this question. Several experimenters have proved that in animals injuries of the nervous system will produce a rise of temperature, and in a recent paper⁴ I have given references to all these experiments, and have shown that lesions of the corpus striatum and optic thalamus will, in rabbits, cause a great rise of temperature quite apart from the influence of the anæsthetic and the operation, but that lesions of the neighboring white matter probably do not influence the temperature. Dr. Goodhart⁵ has published cases which he calls examples of inordinate fever, and which he suggests are due to a functional disturbance of the cerebral heat-regulating mechanism, and I have recorded⁶ some similar cases under the name of inexplicable pyrexia, and have also published an example of hysterical pyrexia.⁷ In an article⁸ on the neurotic theory of pyrexia, I tried to show that all pyrexia must be either primarily neurotic—that is to say, due to a lesion of the central nervous system, or the paths from it to the muscles, which are the chief thermogenetic tissues, an instance of this variety of pyrexia being that which is sometimes found associated with tumors of the brain; or it must be due to a reflex affection of some part of the heat-mechanism, probable instances of this are the rise of temperature produced by a small tense abscess, and that sometimes induced by the colic due to gall-stones; or it must be due to the stimulation of the nervous heat-mechanism or the muscles by the circulation of some poisonous products through them or through some part stimulation of which affects them reflexly. An instance of this form of pyrexia may be the rise of temperature which accompanies zymotic diseases and belladonna-poisoning; and possibly, also, sometimes the poison acts on some part of the thermolytic mechanism. In 1887, Dr. MacAlister, in his *Gulstonian Lectures*,⁹ fully endorsed the view that the nervous system controls pyrexia. He pointed out that the mechanism probably consists of three parts. They are a heat-loss or thermolytic mechanism acting chiefly through the skin by the cutaneous vessels and sweat-glands; its centre is in the medulla; a heat-production or thermogenetic mechanism which consists

¹ Guy's Hospital Reports, vol. xlii. p. 49.

² *Lancet*, July, 1885, June, 1889.

³ *Therapeutic Gazette*, September 15, 1867; *Brain*, 1889; *Journal of Nervous and Mental Diseases*, 1884 and 1887.

⁴ *Journal of Physiology*, vol. xi, No. 1.

⁵ Guy's Hospital Reports, vol. lxx. p. 379.

⁶ *British Medical Journal*, 1886, vol. xi. p. 1096.

⁷ *Clinical Society's Transactions*, vol. xix. p. 124.

⁸ *Practitioner*, January, 1886.

⁹ *The Nature of Fever*, 1887.

of (a) the muscles in which the greater part of the heat of the body is produced, or (b) that part—probably the corpus striatum—of the cerebral nervous system which controls this function of the muscles, and of (c) nervous paths connecting these two parts. Lastly, a thermotaxic mechanism, whose office is to adjust the balance between the other two; the seat of this mechanism must be in the nervous system, but its precise position is unknown.

Dr. MacAlister, toward the end of his lectures, observed that the thermotaxic mechanism was almost certainly the last of the three to be evolved, therefore it is the most difficult to localize. It is very elementary in children, and hence the frequency with which in infants slight causes produce considerable pyrexia, and it is easily disturbed through a wide range, as we see in hysterical pyrexia. The thermolytic is the first to be developed. It is well organized, and definitely localized in the vasomotor, respiratory, and sudorific centres; even cold-blooded animals have a thermolytic mechanism. The thermogenetic mechanism is developed after the thermolytic; it is fairly definitely localized, and is first met with well developed in warm-blooded animals. The nervous heat-mechanism, therefore, follows the law of evolution, consisting, as it does, of the passage from the most to the least organized—that is to say, from the lowest well-organized centres up to the highest least-organized centres. The order of organization is like that of evolution—thermolytic, thermogenetic, thermotaxic. Fever, MacAlister looks upon as a dissolution—first, of the thermotaxic, then of the thermogenetic, and lastly, of the thermolytic mechanisms; and he considers that during recovery, first the thermotaxic, then the thermogenetic, and finally the thermolytic recovers.

The above abstract, I think, fairly represents our certain knowledge, and also the modern theory of pyrexia. I propose now to indicate some facts which support this theory, and to examine those that have been urged against it.

The above theory of the evolution of the heat-mechanism supposes the thermolytic is much earlier evolved in the animal scale than the thermogenetic mechanism, and this is supported by the fact that cold-blooded animals are much lower in the animal scale than warm-blooded; for, as warm-blooded animals have to maintain a fairly constant temperature however cold their surrounding medium, we should expect that they would have a much more potent heat-producing mechanism than animals whose temperature fluctuates with that of their environment. It struck me that if the corpus striatum presides over heat-production it ought to be much larger in warm-blooded animals than in cold. I referred to the text-books on comparative anatomy, and although the information is scanty, it appears that this body is small in fishes and amphibians, is larger in reptiles, and becomes much bigger in birds.

We thus see that, roughly speaking, the corpus striatum is smallest in cold-blooded animals and largest in warm-blooded. Further observations on the subject are required—perhaps it will be found that it is largest in just those reptiles, such as the *Python bivittatus*, which are warm-blooded. In birds it is especially large, and this is interesting when we bear in mind the high temperature they often maintain.

Again, if this evolutionary view be correct the thermotaxic mechanism should be better developed in man than in lower mammals. I made a series of observations upon the rectal temperature of twenty-seven rabbits, and found that quite commonly the temperature varied between 101° and 103° F., and in some few animals a little beyond these limits, so that we may fairly say that the range of normal rectal temperature in this animal is three degrees, a much greater range than in man. It seems rational to attribute this difference to the fact that probably in the rabbit the thermotaxic mechanism is not so well developed as in man.

Also, this evolutionary view appears to derive support from the action of drugs. The materia medica books all state that those drugs which increase the perspiration and dilate the cutaneous vessels, reduce the temperature. Such are alcohol, nitrous ether, and antimony; but every clinical physician knows that these drugs are most uncertain in their antipyretic action, and as a rule have very little effect. Drugs, however, such as quinine, antipyrine, etc., which certainly do not act through the thermolytic mechanism, and, therefore, must act upon one of the other two mechanisms, are powerful agents in reducing pyrexia.

Sawadowski states that antipyrine most certainly acts upon the corpora striata, for after the removal of these bodies in dogs its antipyretic effect could not be observed. If these experiments are confirmed, as, judging from other experimental work, they probably will be, we may conclude that antipyrine acts by diminishing thermogenesis. We, therefore, see that it is difficult to influence by drugs the earliest developed, the thermolytic mechanism, but it is comparatively easy to act upon those—the thermogenetic and thermotaxic—which are later developed. This, however, is nearly always the case with drugs. For example, the recently developed mental faculties are much more easily acted upon by alcohol than are the earlier developed functions, such as motion, respiration, etc.

Another fact in favor of this view of the order of evolution of the heat-mechanism is the circumstance that young children quickly become cold if artificial warmth be withheld. The difficulty of keeping infants born prematurely properly warm is well known, and it is not improbable that the *fetus in utero* is, until quite the late months of pregnancy, a cold-blooded animal depending for its warmth on the surrounding warmth; and this points to the order of evolution already mentioned.

Against the view that because the chief centres for the vessels of the

skin, for the sweat-glands, and for the respiratory movements, are in the medulla oblongata, and that therefore this part of the central nervous system presides over the thermolytic mechanism, it has been urged that some of the variations of temperature which are produced by cerebral lesions higher up may be due to altered thermolysis, because parts of the higher central nervous system have been thought to have some vasomotor influence, and because sometimes there is a unilateral altered secretion of sweat in ordinary hemiplegia. But it is to be remembered that the vasomotor effects of hemiplegic lesions are insignificant compared with the severe vasomotor disturbance which follows upon lesions of the medulla oblongata, or of the cord, or of the nerves below it; also, it must be borne in mind that alterations in the amount of sweat secreted, and in the degree of vascularity on the side of the body opposite the lesion in hemiplegia, are very rare, and when they take place they are usually slight. Then, also, if we imagine that the rise of temperature following lesions in the cerebrum is due to altered thermolysis, it is very difficult to explain the fact that a lesion of the cerebrum will in a rabbit sometimes produce a rise of several degrees in the rectal temperature within an hour of the experiment, and after a few hours it may sink equally rapidly, for in animals thickly coated with fur alterations in the internal temperature of the body due to variations in thermolysis can only take place slowly. It is also possible that the rare vasomotor and sudorific effects of lesions above the medulla are not due to the direct influence of the higher nervous mechanism, but to a reflex affection of the vasomotor and sudorific centres of the medulla. We probably see instances of a reflex affection of these centres proceeding from the higher parts of the brain in the blushing from emotion and the sweating from fear that are so common. Lastly, we must bear in mind that there are several instances in which, although a certain part of the central nervous system has for its chief office the presiding over a certain function, yet it has some slight influence over functions which are chiefly supervised by some other part of the central nervous system. For example, the area of the cerebral cortex either side of the fissure of Rolando for the most part presides over the motion of the opposite side of the body, yet if it be damaged, there is some weakness on the same side of the body, and also some impairment of the sensation on the opposite side; these, and similar facts, seem to show that when we speak of having localized a function to a certain part of the brain, all we mean is that it is the part whose chief office is to preside over the same function. Looking at the question in this way it would harmonize with well-known facts to suppose that the cortex has some slight vasomotor and sudorific influence. We thus see that at least two other interpretations are possible of those facts which seem to show that the alteration in temperature which follows some lesions above the medulla may occur because the chief centre

for thermolysis is above the medulla; and we also see that on the whole the evidence is greatly in favor of the medulla being the part of the central nervous system which presides over the loss of heat. Probably former writers did not pay sufficient attention to the frequency of respiration as a means of regulating the loss of heat, for many recent experimenters have shown that an increased warmth of blood leads by its stimulation of the medulla to an increased frequency of respiration, and a consequent increased loss of heat, and that this is one of the thermolytic mechanisms by which the temperature is maintained constant. The medulla has consequently been said to have a thermopolypnoic centre.

We now pass to the thermogenetic mechanism. Most observers who investigated the subject before 1886 came to the conclusion that in fever the heat-production was increased, but it must always be remembered that a patient's temperature is the balance between his heat-loss and heat-production, and therefore it does not by any means follow that when the temperature is raised the heat-production is increased. Since then this supposition has been confirmed, not only by calorimetical observations upon the limbs, such as those of Rosenthal upon the arm, but also by calorimetical experiments upon man. Ott put a man suffering from ague into a calorimeter, and showed that with the onset of pyrexia the production of heat was enormously increased, and Langlois has made over one hundred calorimetical observations upon children suffering from broncho-pneumonia and from varicella, and he also found the heat-production to be increased.

It is worthy of note that in just those two fevers in which high temperature persists longest—viz., typhoid and tuberculosis—the patients waste most, and this in spite of the fact that they are fed abundantly. I have often wondered whether this wasting of the muscles was the result of the very active thermogenesis that takes place in them. Sometimes the association between the wasting and the temperature is so intimate that it is very tempting to assume a close connection between them. To give an example: I saw a patient who had a high temperature as the result of an empyema. He wasted rapidly; the pus was let out, the temperature fell, and he put on flesh at once. After some days the pus re-collected, the temperature rose again, and he began to waste visibly from day to day. The pus was let out for the second time; again the temperature fell, and he put on flesh as quickly as he had lost it. Facts like these are very suggestive, and it is quite possible that some day they may be looked upon as a proof that the muscles are the chief thermogenetic tissues. It may, of course, be asked whether we ought not to get a subnormal temperature in diseases such as pseudo-hypertrophic paralysis, progressive muscular atrophy, and primary muscular atrophy, in which there is great muscular wasting; but it must be remembered that we have very few records of the tempera-

ture of these diseases, that a diminished production may be compensated for by a diminished loss of heat, and also that it is well known in pathology that slow destruction does not abolish function to anything like the extent that a rapid destruction does. We do not know what chemical changes in muscle lead to the production of heat; perhaps the increased excretion of urea in fever has some bearing in this relationship. One cannot help noticing that in hydrophobia and tetanus, both of them diseases in which the motor function of the muscles is profoundly disorganized, the temperature of the body is also raised, occasionally in tetanus to a great degree. But it must not be supposed that this is an argument for supposing that the motor and thermogenic functions of muscle are the same. On the contrary, these diseases show that the opposite is the case, for they are both examples of disorders in which a considerable post-mortem rise of temperature may take place after all movements of the muscles have ceased. It is hardly possible that this could occur unless the production of heat continued after death; therefore in these maladies we have an instance of the continuance of one function of a muscle after the cessation of the other.

I have already alluded to the many clinical facts and to the experiments, several of which have been calorimetric, that have accumulated during the last few years, and which show that damage to the corpus striatum or to the optic thalamus increases the production of heat. Against this view it has been urged that it is extremely unlikely that two bodies, developmentally so different, should have a similar function; but probably this similarity is more apparent than real, for it is quite possible that a lesion of the optic thalamus may injure the tail of the caudate nucleus, or that part of the lenticular nucleus which lies to the outer and under part of the optic thalamus. The corpus striatum may developmentally be regarded as part of the cortex, and therefore it is reasonable to suppose that it, like some other parts of the cortex, has a localized function. The previous experiments in favor of its thermogenic function have been confirmed by those of Sawadowski and Ott, both of whom have shown that when putrid blood is injected into the veins it is impossible to induce fever if the corpora striata have been removed.

Whether it restrains or stimulates heat-production in health is at present a doubtful question; but the balance of evidence is that the corpus striatum is not inhibitory, for Messrs. Aronsohn and Sachs¹ found they could, by carefully stimulating it by an electric current, always produce a rise of temperature in the muscles and rectum. In these experiments the damage to the surrounding parts was very slight, and every time the current was passed the temperature rose. These results

¹ Pfüger's Archiv, 1885.

were published in 1885, and were quoted by Dr. MacAlister in 1887. In 1884, in my paper in the *Guy's Hospital Reports*, I argued that the thermogenetic centres were inhibitory in their action, and that when they were damaged the temperature rose because this inhibitory power was paralyzed. Since then a consideration of Messrs. Aronsohn and Sachs's experiments, of some of my own, and of fresh clinical facts, leads me to the conclusion that the hypothesis I put forward in 1884 was probably wrong, and that damage to the corpus striatum causes the animal's temperature to rise because the lesion irritates that organ. In favor of this view is the fact that a very small lesion of the corpus striatum will cause a considerable rise in temperature. I have seen a mere puncture in rabbits and a minute patch of softening of the corpus striatum in a human being cause a great rise of temperature, certainly suggesting that mere irritation will greatly increase the production of heat. On the other hand, both in artificial experiments and in the human subject, sometimes the destruction has been extensive and a high temperature has resulted; but it must not be forgotten that a lesion can hardly, unless it kill the animal or the patient, be sufficiently large to destroy the whole of the corpus striatum, and that if only part is destroyed the lesion will irritate the remainder. It is a remarkable fact, which I have often verified, that if in a rabbit a rise of temperature has been produced by a lesion of one corpus striatum, and after the temperature has fallen to normal the other corpus striatum is damaged, the temperature rises again, but it does not remain raised, but falls in a few days. This fact is strongly in favor of the view that the lesion causes a rise of temperature by its irritative effects. I have recorded the case of a child, in whom the temperature was raised often to a great height at frequent intervals for many weeks. At the autopsy the only lesion discoverable was a minute patch of softening in each corpus striatum, which might very well have been a powerful irritant, but certainly destroyed very little of these bodies.

Whilst there is thus a good deal of sound evidence, both experimental and pathological, of the locality of those parts of the nervous system which preside over thermolysis and thermogenesis, we have no certain knowledge of the position of the thermotaxic part which in health maintains the balance between these two, but no evidence has been brought forward to show that it is improbable that any part of the central nervous system has a thermotaxic function. There is, however, clinical evidence of the existence of this function, for although a few years ago those who talked of hysterical pyrexia were often laughed at, now its existence is allowed, and a description of it has crept into two English text-books—viz., Dr. Payne's *General Pathology* and Dr. F. Taylor's *Practice of Medicine*—and it is probably an instance of a disturbance of the thermotaxic mechanism. The chief reasons for this view

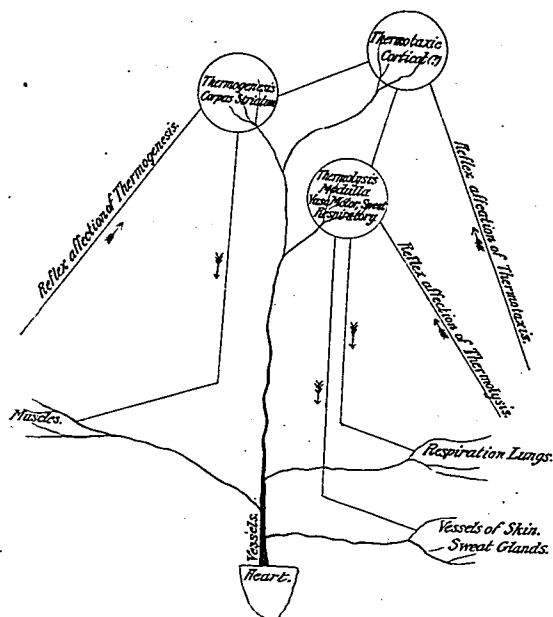
are the extreme and sudden irregularity of the temperature—often it will vary several degrees in an hour; its great height, a height which would probably be fatal if caused solely by an increased production of heat; the fact that it may be very high without the usual accompaniments of a high temperature; and, lastly, the circumstance that the latest evolved mechanisms are on the whole more likely to be upset functionally than are those which are more fixed. It is often the case, that in diseases in which the temperature has ranged high, shortly before death it runs up abnormally high. This is possibly evidence of the existence of a thermotaxic mechanism, for one cannot help suspecting that this mechanism which has been struggling hard to maintain the balance between the heat-production and heat-loss suddenly becomes paralyzed from overstrain, and the temperature at once rises. Rheumatic hyperpyrexia is probably another instance of disorganization of the thermotaxic mechanism.

Our knowledge of the position of this mechanism is very scanty; probably, as it is functionally and developmentally higher than thermolysis and thermogenesis, its seat is anatomically higher, and therefore we should look for it in the cortex. If this is so, it may explain the rise of temperature which many observers, such as Landois, Wood, and Ott, have obtained in experiments upon the cortex. The latter observer is definitely of opinion that the cortex in the region of the fissure of Rolando contains thermotaxic centres, but he also believes that there are some at the base of the brain.

I know of two cases which afford support to the view that the thermotaxic centre is cortical. One¹ has been already published. It is the case of a man who shot himself in the head with a bullet, and was admitted into the hospital unconscious. The bullet was immediately extracted. The temperature after the operation was 99.2°; four hours afterward it had mounted five degrees, to 104.2°. It remained high till the patient died, twelve hours after the operation. It was found that the dura mater was not perforated; the lesser wing of the sphenoid was broken, and parts of the ascending parietal and third frontal convolutions were severely bruised, but otherwise the brain was healthy. Here we have a case in which the thermolytic and thermogenetic centres were not injured, yet there was a rapid rise of temperature—more than a degree an hour—continuing after the bullet was removed, and taking place so immediately after the wound and the operation that the combined shock—which of itself would tend to depress the temperature—of these two could not have passed off. These facts make one strongly suspect that the thermotaxic mechanism was deranged, more especially as other higher centres were disorganized, for the patient was admitted unconscious, and remained so till he died.

¹ Guy's Hospital Reports, 1884, p. 91.

My other clinical case, which appears to localize thermotaxis in the cortex, is that of a man with meningitis, who died within twenty-four hours of the onset of the first symptom, and who had hyperpyrexia, the temperature, which reached 110° F., for two or three hours rising at the rate of two or three degrees an hour, and this, at one part of the rise, in spite of the fact that he was being sponged with ice-cold water. The meninges were acutely inflamed, and it does not seem improbable that the irritation caused by the meninges disorganized the cortical thermotactic function.



We may, therefore, I think, conclude that the theory of a heat mechanism and its evolution, stated in the first part of this article, has many facts in its support, and there are none which disprove it. Throughout this paper the word centre has been used in its ordinary meaning; although it is a word which should be avoided, it is often difficult to find a substitute. Both the thermogenetic and the thermo-

lytic centres and their efferent nerves are probably both anabolic and katabolic, but for the sake of simplification this subdivision has been omitted.

The accompanying diagram is intended to show that the thermolytic mechanism acts chiefly through the lungs and skin, and the thermogenetic chiefly through the muscles; that the thermotaxic maintains a balance between these two; that either centre can be affected reflexly, and that all parts of the mechanism can be influenced by the quality of the blood circulating through them.

CASE OF AORTIC ANEURISM PRESENTING ONLY INDIRECT SYMPTOMS.

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J. B., aged thirty-six years, by trade a driller, was admitted to Ward 11 of the Western Infirmary on November 16, 1889, complaining of hoarseness of four months', cough of two months', and expectoration of six weeks' duration.

He stated that he caught a chill in the end of June, and two days afterward was attacked with hoarseness. The doctor who examined him could detect nothing in the throat, and he therefore neglected the hoarseness, which remained unchanged. Two months before admission cough began, for which he was "painted" with some external application. This gave no relief, and shortly afterward he had to stop work owing to the severity of the cough, which was frequently so great as to produce vomiting. Expectoration of a clear, thick sputum also began about two weeks afterward. Since the onset of his illness he has been subject to night-sweats, but there has been only slight emaciation. The bowels are moved twice daily. Appetite is good. He has never had any pain in the throat or chest. He suffers from palpitation and shortness of breath—both being worse on exertion and relieved on sitting or lying down.

On examination there are found indications of commencing consolidation at the right apex, and at the left prolongation of expiration, with sibilant râles. The expectoration, which is frothy and muco-purulent, contains no tubercle bacilli. Over the whole left lung, back and front, the respiratory murmur is much weaker than on the right side.

The heart-sounds are normal. The apex-beat is not displaced, nor is the dulness enlarged. Both radial pulses are equal.

The left pupil is dilated and fixed, but the fundus is normal, while the right optic nerve is pale and cupped at its margin.

The voice is replaced entirely by a whisper, and the cough is "incomplete" and laryngeal in character. On examination of the larynx the left vocal cord is found to be paralyzed in the cadaveric position.